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Some observations on proton magnetic resonance in hydrogen-bonded systems

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With 17 figures in the text

Introduction

The original work of Bloch, Purcell and their respective collaborators on the magnetic resonance of nuclear spins [1, 2] as contained in bulk matter has opened such a vast and ramifying field of investigation that the information and knowledge that these novel methods are now furnishing us are mostly related directly or indirectly to the molecular and immediate electronic environments around the nucleus, even though the phenomenon itself is directly of nuclear origin. As the molecular and electronic environments around the nucleus basically govern the success of the observation of the nuclear signals through the mechanism of the spin-lattice interaction, it was apparent that these methods of "nuclear induction" and "nuclear magnetic resonance absorption" should be of immense importance in the investigations of all phenomena and effects concerned with the molecules in which the nuclei are embeded. Although the studies of nuclear spin-lattice relaxation time gave valuable information on molecular motions and other inter- and intra-molecular parameters and effects in solids, liquids and and gases, it could however not provide much information concerning the internal structure and other features of the molecule depending on the electronic environment of the nucleus which is responsible for the building up of atoms and molecules.

Bloch and his collaborators [3] have ingeniously extended the scope of the applicability of the "nuclear induction" method just in these directions by opening a new section known as "The high resolution nuclear magnetic resonance spectroscopy" which has brought to light many hitherto unknown facts and illuminated many other unsolved problems concerning the nucleus–electron system in the molecules.

This high resolution n.m.r. method is not only offering us a better insight of the molecule but also giving us interesting information on molecules which form molecular complexes. Such formation of molecular complexes, termed also as "molecular association", which we shall discuss in some detail later, is essentially due to some characteristic feature of the hydrogen atom, known as "hydrogen bonding". The liquids in which molecules exhibit such bonding are carboxylic acids, alcohols and many other organic compounds are termed as associated liquids. In this communication we shall describe and discuss some observations on proton magnetic resonance in certain systems where in some cases the hydrogen bonding exists within the molecule itself as characterised by the name intramolecular association.

Various physical methods such as infra-red and Raman spectroscopy, dielectric and electric dipole moment measurements of molecules and magnetic susceptibility measurements of molecules have also been applied to study molecular association. Since in the phenomenon of molecular association it is the hydrogen atom which plays an all-important role by virtue of hydrogen bonding, it is necessary and should be of value to study proton magnetic resonance in all systems where such bonding exists and also in processes where such bonding comes into being as in the formation of new molecules, e.g. in chemical reactions. These n.m.r. studies will certainly supplement our knowledge on such systems as gained by other physical methods mentioned above, although the n.m.r. method has some limitations as we shall discuss later. However, the method being a purely physical one, these studies will also enlighten the question whether such systems or some characteristic properties associated with them may reflect some difference when they are being investigated by physical or chemical methods. Further in these n.m.r. studies, since it is necessary to subject the system to a magnetic field, the question of the effect of magnetic field on some observables associated with such systems can be considered and such consideration may bring out new facts. We shall also discuss these points in this communication.

In the studies of molecular association and hydrogen bonding by the technique of high resolution n.m.r. [4, 5, 6], one is concerned with the changes in the so-called "chemical shift" of the proton of the hydrogen atom when entering into such bond formation. Such shift is also termed the hydrogen-bond shift in n.m.r. studies. Although this technique is usually employed some attempt has been made to deduce information about molecular association from spin-lattice relaxation time measurements. As has been mentioned earlier since spin-lattice relaxation is partly dependent on the electronic environment of the nucleus and since the "chemical shift" is directly dependent on it, it seems that the work of Giulotto *et al.* [7] on relaxation time measurements of protons in the ethyl alcohol (C_2H_5OH) molecule from the molecular association point of view seems to be worth mentioning here, although there are certain points which need more discussion. From their measurements they concluded that in the event of molecular association the volume of the molecule or in better words the size of the molecular cluster increases, thereby affecting the Debye correlation time and hence also the rotational contribution of the molecule to the thermal relaxation time. In these spin-lattice relaxation time measurements the relaxation time includes the net effect due to all protons in the molecule, i.e. the protons of the OH group and C_2H_5 group of the ethyl alcohol molecule. But as we know, it is the proton in the hydrogen atom of the hydroxyl (OH) group that is responsible for the hydrogen bond formation and molecular association. The relaxation time measurement is not confined to the proton associated with hydrogen bonding, whereas in the high resolution n.m.r. studies we observe directly the changes in the nuclear signal of the particular proton associated with the hydrogen bond.

Zimmerman [8] has also made some studies of proton relaxation time from the point of view of complex-ion formation and the proton exchange mechanism. Arnold [9] in his detailed studies of the fine structure of proton magnetic resonance in ethyl alcohol also advocates the proton exchange mechanism for the obliteration of the fine structure of the proton resonance line of the hydroxyl group, which according to him may throw some light on hydrogen bonding in ethyl alcohol.

Although hydrogen bonding studies by the magnetic resonance method have been stimulated due to the recent development of the high resolution technique, a very early suggestion of hydrogen bonding in hydrogen fluoride was made by Lindström [10] during his investigations on measurements of magnetic moment of the fluorine nucleus. It was also in this connection of the precise determination of nuclear magnetic moment of fluorine that the "chemical shift" in the n.m.r. phenomenon was first suggested by Siegbahn and Lindström [11]. Subsequent experiments by Lindström, taking different fluorine-containing chemical compounds including hydrogen fluoride, led him to state that the difference in resonance frequencies of the fluorine nucleus for different compounds is dependent on the nature of bonding around the fluorine nucleus and that in hydrogen fluoride several molecules associate together by virtue of the hydrogen bond of the type H–F–H.

As we are interested in this communication in the high resolution n.m.r. studies of molecules which exhibit molecular association by virtue of hydrogen bonding, we have thought it worth while to discuss in brief some relevant points of the phenomenon of molecular association, its early concept, its studies by different physical methods and its bearing on recent n.m.r. studies.

Hydrogen bonding and molecular association vis-à-vis n.m.r and other studies

The phenomenon of molecular association [12, 13] has interested scientists since the later part of the last century ever since anomalies in the molecular weight determination from lowering of freezing point of liquids were observed. The pioneering ideas of Louis Henry regarding molecular association and the earlier work of Eötvos, Ramsay and Shileds, Nernst, Trouton, Guye, Bertholet, Turner, Traube, Longinescu, Walden etc. may be noted here, as well as more recent works on association by Auwers, Sidgwick, Latimer and Rodebush, Pauling and Brockway, Lassettre, Smith, Wulf and Liddel and others. Earlier work, however, did not throw much light upon the true nature of molecular association and often conflicting ideas and hypotheses were put forward to explain this phenomenon. Mention may be made of the hypothesis of Longinescu and Chaborski [12] in which they considered the phenomenon of molecular association as one of molar concentration, thereby replacing the idea of molecular complexity by the idea of simple molecular accumulation or crowding of the molecules into a given volume. They stated, "instead of modifying the nature of the molecules by their association, we modify their number in unit volume, while preserving their simplicity". They had some success in accounting for the deviations observed in cryoscopic, capillary and other measurements. They considered that molecular accumulation was being caused by molecular attraction, but by their attempt to preserve the simplicity of the molecules, they denied the existence of any actual bond between two constituent atoms of two or more different molecules.

Observations from nuclear magnetic resonance studies and other methods such as infra-red and Raman spectroscopy, electric dipole moment measurements, electron difraction studies etc., prove the definite bonding between single molecules to form molecular complexes and not merely "molecular accumulation". From early work on dielectric constant and electric dipole moment measurements of molecules, Smyth [14] and others attributed the cause of intermolecular action leading to molecular association to the electric dipole of the molecule. It may be mentioned here in passing that the interpretation of molecular association on the basis of electrostatic attraction between dipoles is, however, not sufficient and the energy of the hydrogen bond is not purely electrostatic in origin. The molar polarization due to the permanent electric dipole moment of the molecules denoted by P_m, is given by $4\pi N\mu^2/9\,kT$, where the symbols have their usual significance adopted in dielectric studies. When two such polar molecules (doublets) associate with their moments pointing in opposite directions, the moments cancel one another and the doublet contribution to P_m becomes zero. In dilute solutions of such a polar liquid dissolved in a non-polar liquid (say benzene or carbon tetrachloride), the orientation of the polar molecules relative to one another may change, and such changes will have a definite contribution to P_m. This was the underlying principle in studying the phenomenon of molecular association from electric moment measurements. Such early dielectric studies led Smyth and Rogers [15] to state, "when the polar molecules are in very dilute solution and on the average far away from one another, they should assume a random orientation unless they actually associate to form complex molecules which are not dissociated even in the dilute solution, as appears to be the case with acetic and butyric acid in benzene". Their determination of P_m to be zero for acetic acid justified their assumption of actual double molecules of acetic acid. Our nuclear magnetic resonance studies [4] also supports the view that acetic acid in benzene solution exists as double molecules. Electric dipole moment measurements of molecules, we thus see, support the view of molecular complex formation as opposed to the hypothesis of simple molecular accumulation.

Dielectric constant and electric dipole moment measurements on various alcohols also suggest molecular association in those liquids. However it may be mentioned here that the types of bonding which lead to molecular association in alcohols and in carboxylic acids differ in some respects. In these studies, as in nuclear spin–lattice relaxation time measurements from the molecular association point of view, it is an effect due to the molecule as a whole that is observed and the observation here is not directly concerned at the seat of the bonding for which molecular association occurs. In this respect, however, the infra-red and Raman spectroscopic studies have the directness of approach to observe the changes accompanying the stretching frequency of the O–H bond wherein lies the seat of hydrogen bonding. Infra-red and Raman spectroscopic studies [16] have proved that molecular complex formation not only exists in carboxylic acids and alcohols, but in other compounds, e.g. phenols, ammonia, all compounds containing amino groups etc. Molecular association in all compounds is due to a characteristic feature of the hydrogen atom which is attracted by rather strong forces to two atoms instead of only one, so that it may be considered to be acting as a bond [16] between them. The credit of propounding the hydrogen bond goes to Latimer and Rodebush [17] who proposed that under suitable conditions the hydrogen nucleus can partake in bonding between two atoms. The hydrogen atom with the only stable 1*s* orbital can form only one covalent bond with another atom, so that the bonding with the other atom in the hydrogen bond is ionic in nature and is therefore represented as X–H...Y, the dotted line carries the ionic sense and X and Y may be different or like atoms. It is now well known that most electronegative atoms enter into hydrogen bond formation and that the strength of the bond increase with increase in the electronegativity of the two bonded atoms. Referring to the electronegativity scale, we might expect that fluorine, oxygen, nitrogen etc. would possess this ability to an extent decreasing in this order. It is actually found that fluorine forms very strong hydrogen bonds and the association in hydrogen fluoride may lead to an agglomeration of many molecules giving rise to a polymer represented by $(HF)_n$, as we mentioned earlier from Lindström's observations [10] on magnetic moment measurements of the fluorine nucleus.

Proton magnetic resonance studies of ammonia by Ogg [18] and an explanatory note on some of his observations by us [19] justify the existence of hydrogen bonding and molecular association in ammonia. Here it is the nitrogen atoms which are entering into such bonding. Hydrogen bonding where oxygen atoms are taking part are very well known as in the case of carboxylic acids, alcohols and phenols. The type of hydrogen bond in carboxylic acids, however, differs from that found in alcohols in several important respects [20]. It is of much greater strength in the acids, as is shown both by the energy of the bond and by the fact that association may persist even in the vapour phase, an effect not found in alcohols and water. Hydrogen bonding in water has been investigated by Shoolery and Alder [21] by high resolution n.m.r. studies on aqueous solutions of diamagnetic salts, and they have interpreted their observations by the ability of the ions to polarise the water molecule and to break down the hydrogen bonds between the water molecules. Water is also known as a hydrogen bond forming solvent. Hydrogen bond formation between solute and solvent molecules were suggested from early experiments of molecular weight determinations by Meldrum and Turner [22] who found that compounds which are least polymerized in benzene tend to be most polymerized in water. This is due to the fact that hydrogen atoms of water can enter into hydrogen bond formation with molecules of the solute. This is exactly what we have conceived in the proton chemical shift curve of the acetic acid–water system [4, 5] where water molecules and acetic acid molecules form molecular complexes by virtue of hydrogen bonding. We shall refer to this question later in this communication while describing our experiment on proton chemical shift of COOH group in an acetic acid and heavy water system.

While discussing hydrogen bonding in water, it would be worthwhile to mention some of the discrepancies which have been observed by Chiarotti and Giulotto [23] in proton thermal relaxation time measurements in water, especially in the case of dissolved oxygen. The paramagnetic influence of oxygen molecules in decreasing the thermal relaxation time of protons in water was first observed by Bloch *et al.* From Chiarotti and Giulotto's subsequent observation the μ_{eff} of the O_2 in the thermal relaxation process was found to be 1.2 Bohr magnetons, in contrast to the value of 2.8 Bohr magnetons of the magnetic moment of the oxygen molecule. It seems that there must be some mechanism other than the paramagnetic influence of oxygen molecule in lowering the thermal relaxation time of protons in the water molecule. Although Chiarotti and Giulotto advocated that molecular complexes like O_4 molecules (believed to be present in the atmosphere in very low concentration) with zero moment may be formed, it appears that it may as well be suggested that oxygen molecules dissolved in water may affect the hydrogen bonding in water and form molecular complexes with it, thereby affecting the rotational motion of the water molecule and hence the thermal relaxation time of protons in it.

Any specific interaction between solute and solvent molecules via the hydrogen bond, is, however, directly and vividly demonstrated by the high resolution n.m.r. studies of the proton in the hydrogen bond. This has been convincingly shown by Huggins, Pimmentel and Shoolery [24] in the case of chloroform, where it enters into specific interaction via the C–H bond with solvent molecules like acetone. As stated above, the strength of the hydrogen bond depends on the electronegativity of the atoms bonded to the hydrogen atom. From the electronegativity scale it would appear clear that the hydrogen-bond-forming power of a hydrogen atom in a C–H bond would be negligibly small. Infra-red studies of the deuterochloroform-solvent system were not so definite in establishing such a bonding interaction, whereas it is only recently that the n.m.r. studies by the above named authors have clearly shown that chloroform–solvent interaction predominantly involves the hydrogen atom of the C–H bond in hydrogen bonding. However, there are certain limitations in the high resolution n.m.r. studies as compared to electron diffraction and especially infra-red studies which we shall mention after some discussions on certain relevant questions on the "chemical shift" effect in the n.m.r. phenomenon.

It should be mentioned here that hydrogen bonding can take place not only between neighbouring molecules, but it can also exist between atoms in the same molecule. In the former case it is called inter-molecular association and in the latter case it is called intra-molecular association. Studies of different systems involving both kinds of hydrogen bonding will be given in this communication.

Chemical shift in the n.m.r. phenomenon

In a previous communication [25] we have presented a general discussion on "chemical shift" and other aspects of studies by the high resolution n.m.r. technique. Here we shall mention only a few points which are related to our experimental observations and other relevant discussions. Chemical shift arising due to interaction of the electronic environment of the nucleus with the magnetic field when it is applied to nuclei residing in different chemical groups within the same molecule, is designated as "internal chemical shift" in order to distinguish it from the total magnetic shielding field considered for nuclei of the same species when they are residing in different molecules, a theoretical treatment of which was given by Ramsey. Although sometimes the chemical shift of a resonance line is referred to that of the proton resonance in water, any effect or parameter associated with the internal chemical shift of a group of nuclei is often best measured from another line arising from a group of nuclei residing in the same molecule, without introducing any other compound into the sample for a reference line. Two different conventions are in practice in expressing chemical shift when it is referred to the resonance line from another compound. Gutowsky and his collaborators express the chemical shift paramater δ as equal to $H_r — H_c/H_c \times 10^5$ where H_r is the magnetic field applied for resonance in an arbitrary reference compound (for example water) and H_c that for the compound in question. Some other investigators, it seems, prefer to express δ as $H_c - H_r/H_c \times 10^6$. Thus the sign and numerical figure of δ will obviously depend upon the notation used and sometimes also upon the compound used as reference. Furthermore it is obvious that δ is also the ratio of the equivalent frequency separation of two resonance lines concerned and the resonance frequency, which is usually held fixed while sweeping the magnetic field. When, from any change in the internal chemical shift of a resonance line, any other quantity is calculated involving the difference and the ratio of two or more chemical shifts during the course of the experiment, it is immaterial whether the shift is expressed in milligauss or cycles/sec or through the parameter δ. This is apparent in the case of the application of the chemical shift effect in following the kinetics of chemical reactions in order to calculate the quantity of the product formed during the reaction, as was shown in a previous communication. It may be mentioned here that in the determination of equilibrium constants of hydrogen bonded systems by chemical shift effects of the n.m.r. method, it is also the ratio of two chemical shifts also called H-bond shifts that are involved. When, however, the exchange rate (say of protons) from the frequency separation of nuclear resonance lines is investigated, it is better to express the chemical shift in cycles/sec.

We shall present here some salient points of Gutowsky and Saika's theory [26] regarding the behaviour of the proton resonance line in cases where protons are exchanging between two molecules, and its bearing on all cases where two molecular configurations are in rapid equilibrium. Such a mechanism not only affects the chemical shift of a proton resonance line, but also the fine structure due to indirect spin–spin interaction within the molecule, as in the case of obliteration of the triplet structure of the OH group of ethyl alcohol first observed by Arnold.

Let us suppose that we have two groups of non-equivalent nuclei of the same species, represented by A and B, present in a system where the nuclei are allowed to exchange between the two groups. The behaviour of the proton resonance from such a system, according to Gutowsky and Saika's theory, will depend upon the life-time of the nuclei in each of the two configurations. If the life-time is long, i.e. if the exchange is slow, the non-equivalent nuclei will constitute two different resonance lines separated by a chemical shift, say $\delta\omega$. If the life-time is short (but long compared to a period for nuclear Larmor precession), i.e. if the exchange is fast, the two resonance lines will constitute a single line depending upon the fraction of protons which A and B contain. They arrived at their result incorporating the chemical shift, (which they denoted by $\delta\omega$) in the Bloch equations describing nuclear magnetization near resonance conditions.

The expression which they present for net nuclear polarization

$$M = \frac{i\,\omega_1 M_0 \left[(\tau_a + \tau_b) + \tau_a \tau_b (\alpha_a p_b + \alpha_b p_a)\right]}{(1+\alpha_a \tau_a)(1+\alpha_b \tau_b) - 1}, \tag{1}$$

where $\omega_1 = \gamma H_1$, γ is the gyromagnetic ratio of the nucleus; H_1, the half amplitude of the radio-frequency field of frequency ω; $\Delta\omega = \gamma H_0 - \omega$, where H_0 is the average resonance field of the two chemically shifted lines; M_0, the equilibrium polarization; τ_a, τ_b the average life-times of the nuclei in group A and group B respectively; α_a and α_b are related to the quantities in the Bloch equations incorporating chemical shift, and are represented below as:

$$\alpha_a = [1/T_2 - i\,(\Delta\omega + \delta\omega/2)] \quad \text{and} \quad \alpha_b = [1/T_2 - i\,(\Delta\omega - \delta\omega/2)];$$

p_a and p_b are proton fractions obviously related to the concentrations of A and B.

Now, in the resonance absorption experiment the imaginary component of the total nuclear magnetization, $M = u + iv$ of eq. (1), is effective. So we shall be concerned with the expression for v for two cases: (I) very slow exchange τ_a, $\tau_b \gg 1/\delta\omega$, and (II) very fast exchange τ_a, $\tau_b \ll 1/\delta\omega$. (Here it is assumed that for discussions in relation to life-times $\delta\omega$ is expressed in frequency units.)

For slow exchange

$$v = \frac{-\omega_1 M_0}{T_2}\left[\frac{p_a}{(1/T_2)^2 + (\Delta\omega + \delta\omega/2)^2} + \frac{p_b}{(1/T_2)^2 + (\Delta\omega - \delta\omega/2)^2}\right]. \tag{2}$$

This gives two resonances with relative intensities of p_a and p_b at $\Delta\omega = -\delta\omega/2$ and at $\omega = +\delta\omega/2$. But for the case of very fast exchange, although the resonance line will be a single line, the position at which Gutowsky and Saika locate it does not seem clear, as the expression for v which they write

$$v = \frac{-\omega_1 M_0/T_2}{(1/T_2)^2 + \omega - (\delta\omega/2)(p_b - p_a)^2} \tag{3}$$

should be

$$v = \frac{-\omega_1 M_0/T_2}{(1/T_2)^2 + [\Delta\omega - \delta\omega/2\,(p_b - p_a)]^2} \tag{3 a}$$

as we find on following their analysis. The conclusion which they drew that the single line should be at $\Delta\omega = \delta\omega/2$ should strictly be $\Delta\omega = \delta\omega/2\ (p_b - p_a)$, but since $p_b + p_a = 1$, $\Delta\omega$ comes out to be $\Delta\omega = p_b\delta\omega - \delta\omega/2$. Now, since they have ingeniously changed the point of reference to the resonance of A at $-\delta\omega/2$, the resonance will now appear at $\Delta\omega = p_b\delta\omega$, which is correct. Thus generally, in the case of fast exchange of protons, the resonance line will be a single one and its position is dependent upon a fraction related to the total number of protons taking part in this exchange mechanism. Not only in the exchange mechanism, will they constitute a single line, but also when protons are present in two different molecular configurations (as in some hydrogen bonded systems) which are in rapid equilibrium. We shall refer to this case later on.

For intermediate rates of exchange the resonance instead of constituting a single sharp line or two lines, may be a broad one, to which case we shall also refer later on in this communication.

N.m.r. observation on reaction between methyl alcohol and acetic anhydride

In a previous communication [27] we have described an experiment showing the possibilities of applying the chemical shift in n.m.r. phenomenon to follow the kinetics of chemical reactions. The method has been extended to study the reaction between methyl alcohol and acetic anhydride. This experiment brings out some more details than the previous one and the analysis of the n.m.r. data shows that the reaction behaves as a second order reaction. The experiment was done at 27°C, the temperature at which the hydrolysis of acetic anhydride was followed by the n.m.r. method. The experiment on reaction between methyl alcohol and acetic anhydride shows that it is slower than the hydrolysis of acetic anhydride.

The reaction is represented by the equation

$$CH_3OH + (CH_3CO)_2O \rightarrow CH_3COOCH_3 + CH_3COOH$$

The reactants being methyl alcohol and acetic anhydride, the final products being methyl acetate and acetic acid. The proton resonance signals from the reacting sample are illustrated in Fig. 1. The proton signals of the OH group of methyl alcohol and of the COOH group in acetic acid constituted a common line, possibly because there is a fast exchange of protons or may be due to formation of molecular complexes which are in rapid equilibrium as a result of which the protons of OH group and COOH group experience an average diamagnetic shielding and therefore

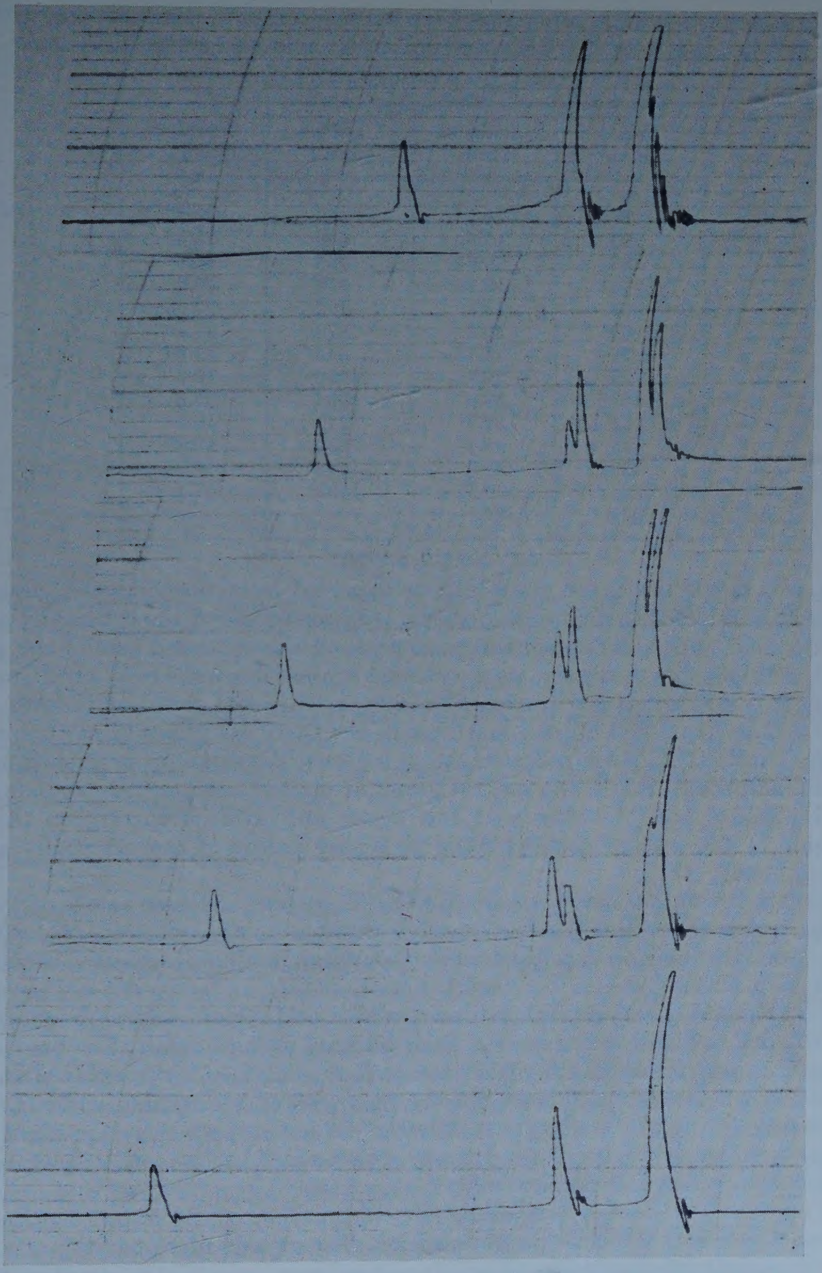


Fig. 1. Picture illustrating the changes in the proton signals from the reacting sample of methyl alcohol and acetic anhydride. For further elucidation see text. The value of the externally applied magnetic field increases from the left to the right in the traces.

Table 1. Chemical shift in milligauss between the common peak shifting with time and the centre of the CH_3 peaks of acetic acid and acetic anhydride (± 0.2 milligauss).

Time (min.)	Chemical shift	Time (min.)	Chemical shift
10	14.2	420	33.95
23	15.6	540	35.52
28	16.64	705	36.4
43	18.85	750	37.0
55	19.8	792	37.08
60	20.3	870	37.6
76	21.45	945	37.96
82	22.7	1080	39.2
132	26.0	1238	39.8
155	27.3	1279	40.3
168	28.1	1380	40.82
180	28.6	1462	40.95
250	30.92	1560	41.4
324	32.1		

constitute a single resonance, as would be expected from the analytical treatment discussed above. This common peak occurs at lower values of the externally applied magnetic field and is depicted as a small peak on the left hand side of the picture where the amplitudes of the signals are plotted against magnetic field which increases from left to right in all the traces. The internal chemical shifts of protons of the methyl groups of methyl alcohol and that in the $COOCH_3$ group of methyl acetate are slightly different. Their positions are in between the common peak shifting with time and the peaks due to the methyl group of methyl acetate (not the one in the $COOCH_3$ group) and of acetic acid and acetic anhydride occurring on the right hand side of the picture corresponding to higher values of the externally applied magnetic field.

The peak due to the methyl group in $COOCH_3$ occurs at lower values of the field than its adjacent methyl peak of methyl alcohol. As the reaction proceeds, the former peak increases in intensity while the latter one due to methyl alcohol decreases with time.

The splitting of the methyl peaks due to acetic acid, acetic anhydride and methyl acetate is due to slight differences in their internal chemical shift. The peak due to the methyl group of acetic anhydride occurred at a slightly lower value of the field than the other groups, as it is seen to be progressively decreasing while the other is increasing during the course of the reaction. In some traces there are slight traces of wiggles which, however, can be clearly differentiated from actual splittings due to difference in internal chemical shift.

The experimental method regarding the observation of the n.m.r. signals is the same as stated in a previous communication. The signals represent the absorption mode of nuclear resonance signals.

Equimolar quantities of methyl alcohol and acetic anhydride were mixed in a bottle, and immediately formed a homogeneous solution unlike the case of acetic anhydride and water in our previous experiment. The experimental observation of nuclear signals was made as quickly as possible. The chemical shift of the common

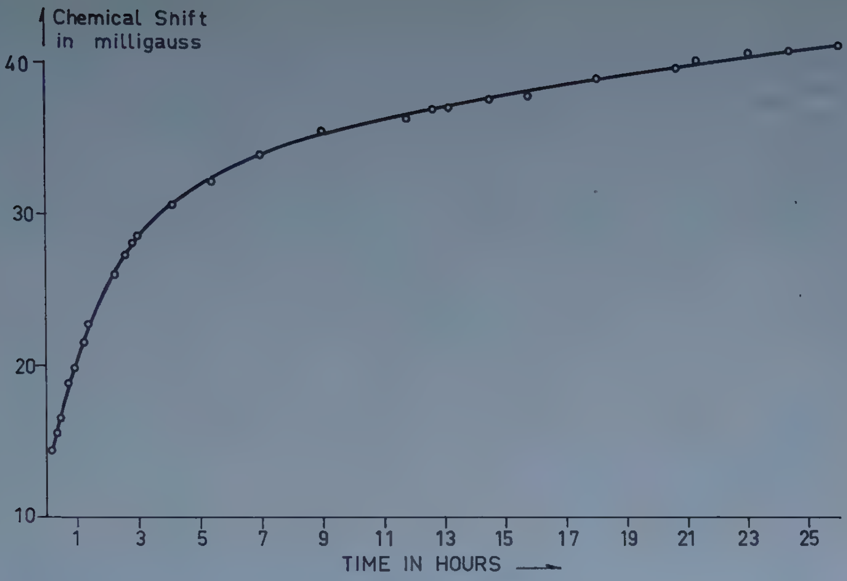


Fig. 2. Curve representing the chemical shift of the common peak due to protons of the OH group of methyl alcohol and the COOH group of acetic acid from that of CH_3 groups of acetic acid and acetic anhydride plotted against time.

peak of OH group of methyl alcohol and COOH group of acetic acid, which changed conspicuously with time, was measured from the centre of the methyl peak due to acetic acid and acetic anhydride. The chemical shift with time is given in Table I and shown graphically in Fig. 2.

Analysis of the n.m.r. data

The procedure used to determine the mole fraction of acetic acid at any time from the n.m.r. experiment is as follows. The curve in Fig. 2 showing the chemical shift of the common peak is extrapolated to $t=0$, giving the position of the proton peak from the OH group of methyl alcohol. Hence, for subsequent times, the chemical shift of the common peak from the proton peak due to the OH group of methyl alcohol can be determined. The common peak, when the reaction is complete, is due to the COOH group of acetic acid and therefore occurs at the characteristic position of the COOH group in acetic acid, which is also known. Now, the ratio of the chemical shift of the common peak at time t, from the peak at time $t=0$, to the chemical shift of the COOH peak in pure acetic acid from the peak at time $t=0$, is equal to the fraction of protons in the COOH groups in acetic acid at time t, which are exchangeable between acetic acid and methyl alcohol or are in rapid equilibrium involving a molecular complex between acetic acid and methyl alcohol. In a methyl alcohol molecule there is one such proton as also in acetic acid, and the molality of methyl alcohol is $a-x$ and that of acetic acid is x and hence the proton fraction in question $x/(x+a-x)=x/a$. This ratio can therefore be determined from chemical shift data and since here $x/2a$ is the mole fraction of acetic acid at any time, as stated below, this quantity is also known. The mole fraction of methyl alcohol

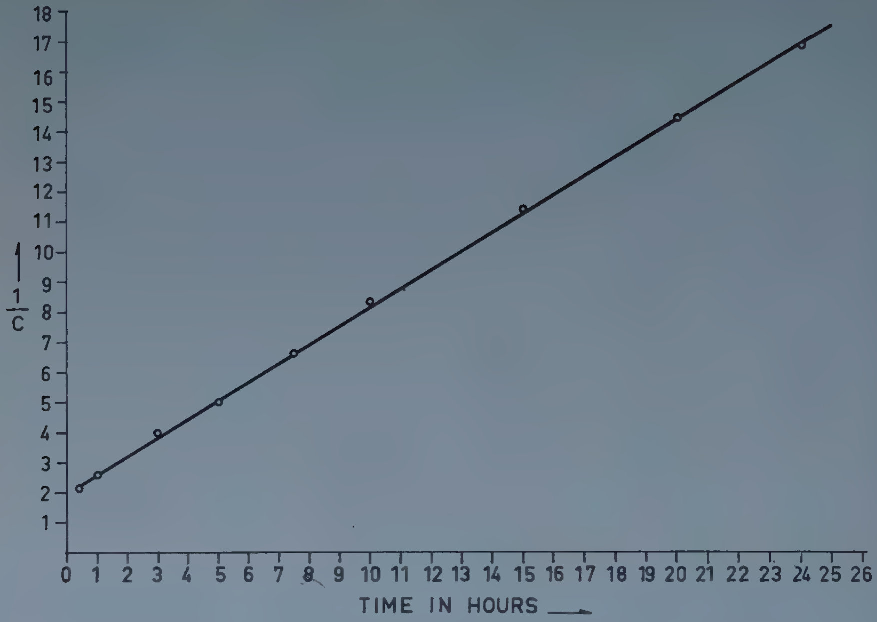


Fig. 3. The reciprocal of the concentration of methyl alcohol (*c*), as calculated from n.m.r. data, plotted against time.

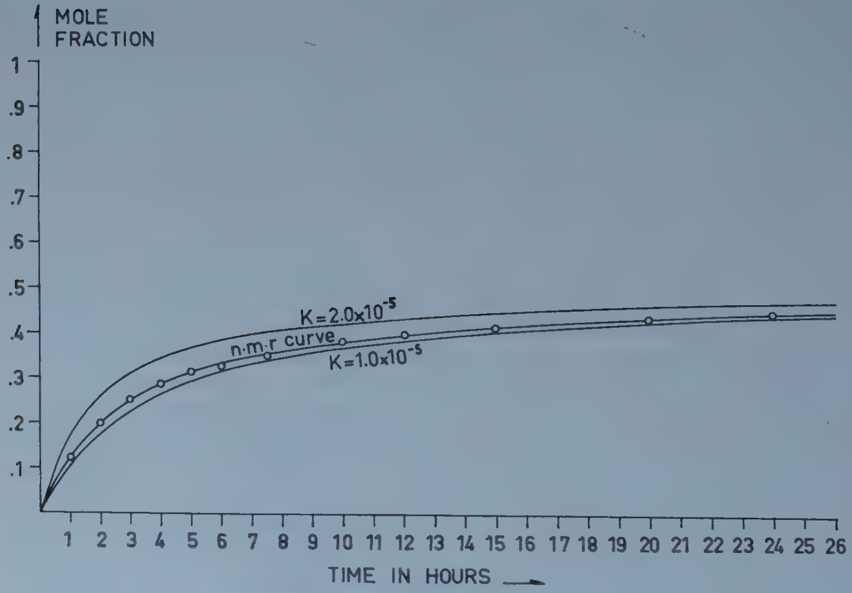


Fig. 4. The n.m.r. curve showing the quantity of acetic acid formed during the reaction and compared with other calculated curves with different assumed values of k_{II}.

(say c) left unreacted at any time can also be determined. Now, when $1/c$ is plotted against time, as shown in Fig. 3, a straight line is obtained showing that the reaction behaves as a second order reaction. The mole fraction of acetic acid evaluated from n.m.r. data is plotted against time in Fig. 4 and compared with different assumed values of the reaction rate constants k_{II}.

If we start with one mole of methyl alcohol and one mole of acetic anhydride per 1000 g of solution, and if we suppose that at time t, x moles of methyl alcohol and x moles of acetic anhydride have reacted, then x moles of methyl acetate and x moles of acetic acid will be formed according to the equation

$$\begin{array}{lcccc} & CH_3OH + & (CH_3CO)_2O \rightarrow & CH_3COOCH_3 + & CH_3COOH \\ \text{Molality} & a-x & a-x & x & x \end{array}$$

The mole fraction of acetic acid at time t is therefore $x/2a$ and that of methyl alcohol $a-x/2a$ (c say).

As we know the initial concentration a, we can determine the values of x at any time for second order reactions with different assumed values of k_{II} from the equation $x/a(a-x)=k_{II}\,t$. Since x is determined, we can calculate the mole fraction of acetic acid $x/2a$ at any time for different values of k_{II} and thus obtain the theoretical values which are plotted in Fig. 4. The agreement of the n.m.r. curve with the second order reaction rate curve is very good. The reaction rate k_{II} is seen to be approximmately 1.2×10^{-5} sec^{-1} molality $^{-1}$.Thus the reaction between methyl alcohol and acetic anhydride is slower than the hydrolysis of acetic anhydride. Some other differences in behaviour of the two reactions in our n.m.r. observations are discussed later.

From the chemical literature it was hard to find any work on the reaction between pure methyl alcohol and acetic anhydride only, from which we could compare our experimental findings by the n.m.r. method. Henion and Vogt [28] were interested in determining by a chemical method the solvent effect on reaction between acetic anhydride and methyl alcohol and their work does not reveal any data on the reaction between pure acetic anhydride and methyl alcohol. However, they found that solvents like chloroform, carbon tetrachloride, ether etc. have a pronounced effect in decreasing the rate of the reaction, which was attributed to hydrogen bonding of methyl alcohol molecules with solvent molecules. Of course, in the case of solvent carbon tetrachloride, hydrogen bond formation between methyl alcohol molecules and carbon tetrachloride does not arise, but this solvent affects the hydrogen bonding between different methyl alcohol molecules, as has been revealed also by magnetic resonance studies by Arnold and Packard [29]. In the reaction of methyl alcohol and acetic anhydride, not only one of the reactants, methyl alcohol, is a hydrogen bonded compound, but one of the products, acetic acid, is also a hydrogen-bonded compound. The solvent effect on the reaction rate from the point of view of hydrogen bonding in acetic acid was not properly considered by them, and their statement, "acetic acid formed may possibly retard the reaction by forming a complex with acetic anhydride", is not correct as we saw in our previous study on the hydrolysis of acetic anhydride. However, Henion and Vogt's consideration of the hydrogen bonding in methyl alcohol molecules in connection with the reaction between methyl alcohol and acetic anhydride seems to be justified.

The effect of temperature and molecular-complex-forming solvent on hydrolysis of acetic anhydride

The fact that molecular complex formation involving hydrogen bonding retards the rate of a chemical reaction is shown in our next experiment, where we have followed the hydrolysis of acetic anhydride in the presence of acetone. Since the final product is acetic acid, and since acetone affects the hydrogen bonding in acetic acid as revealed by another experiment on changes in the chemical shift of the COOH peak, we were interested to see whether the n.m.r. method of following chemical reactions would reveal this retarding effect. As we were also interested to observe by this method the temperature effect on the hydrolysis of acetic anhydride, we have performed another experiment at 22°C to compare the rate with that found at 27°C in our earlier experiment, and the experiment on hydrolysis of acetic anhydride in acetone medium was also done at 22°C. The experimental observations are shown graphically in the same figures. For the experiment in acetone medium, 12.75 g of acetic anhydride, 2.25 g of water and 2.25 g of acetone were used. This mixture assumed a homogeneous phase rather more quickly than the one between acetic anhydride and water only. All other procedures to follow the reaction by the n.m.r. method were the same as described in our previous communication. The chemical shift of the COOH peak at the end point of this reaction in acetone medium is not the same as in pure acetic acid. The chemical shift of the COOH peak in a system of acetic acid–acetone has been observed by us. Huggins, Pimmentel and Shoolery [6] have also observed this shift. In our experiment we took the concentration of acid in per cent by volume, as we were interested also to see whether in this complex-forming process of acetic acid–acetone molecules, the chemical shift curve is of the same nature as in the case of acetic acid–water system. The chemical shift of the COOH peak (termed also as H-bond shift as the shift involves changes in hydrogen bonding), is measured from the methyl peak of acetic acid and expressed

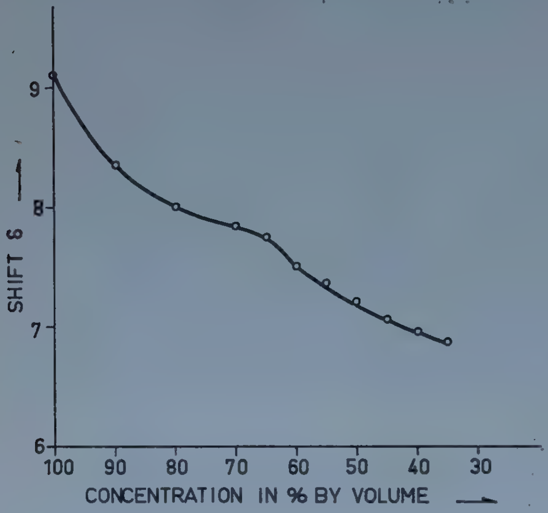


Fig. 5. The H-bond shift of proton resonance of acetic acid in acetone solution plotted against concentration in per cent by volume.

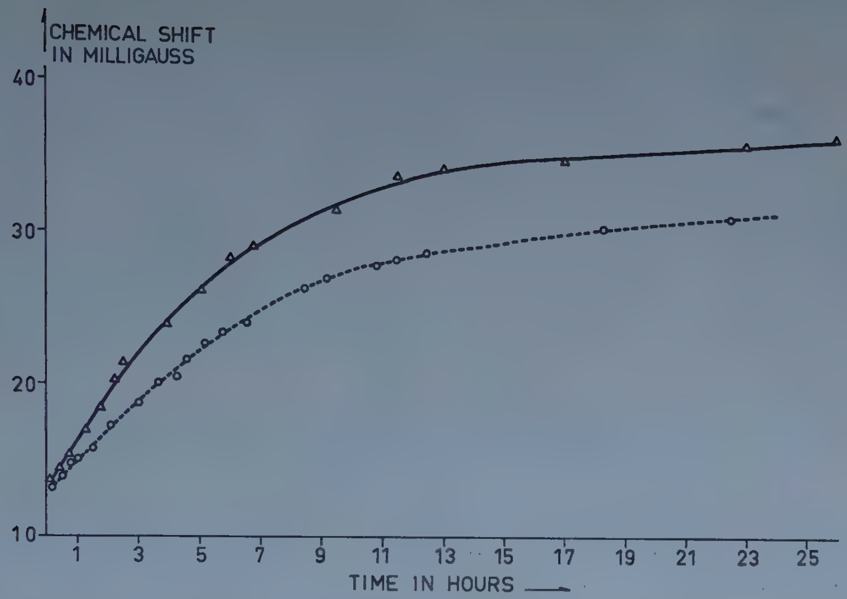


Fig. 6. Solid and dashed curves representing respectively the chemical shift of the common peak due to protons of water and COOH group from that of the CH_3 group of acetic acid and acetic anhydride plotted against time for the experiments at 22°C, for (i) reactants without any solvent, and (ii) reactants with acetone as solvent.

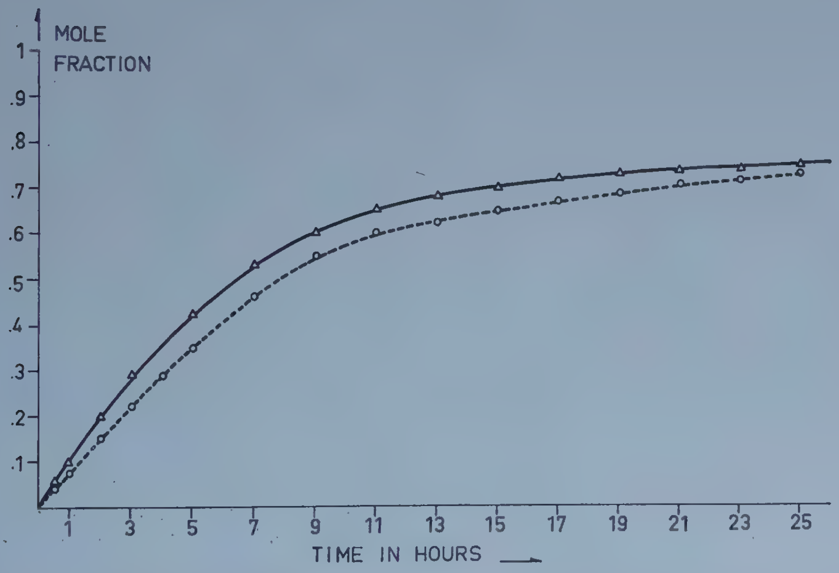


Fig. 7. Solid and dashed curves representing respectively mole fraction of acetic acid present in the reacting system at any time as calculated from n.m.r. data for experiments concerning (i) reactants without any solvent, and (ii) with acetone as solvent.

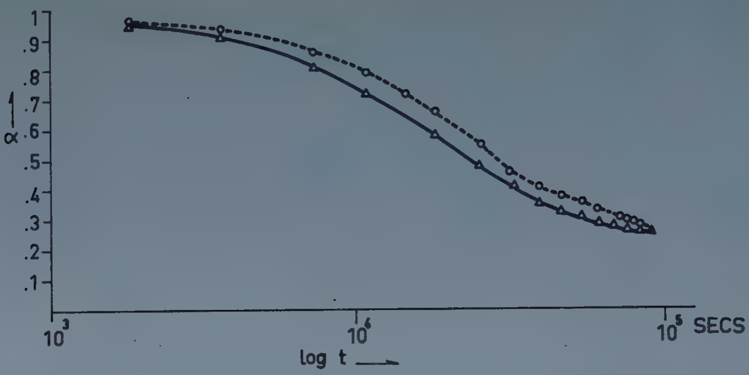


Fig. 8. A plot of the dimensionless quantity α related to the quantity of acetic acid present at any time against log t. For further explanation see text. The solid and dashed curves have the same significance as in Figs. 6 and 7.

as δ, where $\delta = H_r - H/H_r \times 10^6$ in which H_r = methyl proton resonance field and H = proton resonance field of the COOH proton, and plotted against the acid concentration in per cent by volume as shown in Fig. 5.

This curve is also used to determine the shift of the COOH peak from the methyl peak at the end of the reaction from acetic anhydride, water and acetone system. Regarding the observation of the hydrolysis of acetic acid by the n.m.r. technique at 22°C, the temperature of the room in which the experimental equipment was housed was brought down to this temperature by a temperature control arrangement described in our previous communication [25]. In this method, however, it is ensured that the temperature of the reactants when they are mixed and put in the n.m.r. probe is the same as during the course of the reaction. The chemical shift of the common peak, shifting with time, as measured from the methyl peak of acetic acid is plotted in Fig. 6 both for the experiments at 22°C and that in acetone medium, by the solid curve and dotted curve respectively. The mole fraction of acetic acid formed at any time in the reacting system is shown in Fig. 7 for both cases.

The order of reaction for both cases is determined by making a Powell plot [30] by plotting the dimensionless quantity α against the log of time as shown in Fig. 8, where $1 - \alpha$, is equal to the mole fraction of acetic acid present in the system. This method of plotting gives a unique form of the curve for different orders. The shape of the solid curve (in Fig. 8) is characteristic of a first order reaction and therefore it seems that the hydrolysis of acetic anhydride as followed by the n.m.r. method at 22°C behaves as a first order reaction similar to the behaviour at 27°C as was also observed by us earlier. The hydrolysis of acetic anhydride in presence of acetone (shown by the dotted curve in Fig. 8) is also first order to a good approximation but it is seen that towards the end of the reaction there is some deviation, as may be expected from the effect of molecular complex formation between acetone-acetic acid, the deviation being more pronounced with increasing quantity of acetic acid. From the curves in Figs. 6 and 7 it is also apparent that the rate of hydrolysis of acetic anhydride in the presence of acetone is slower than in the case of pure reactants. The reaction rate constants for first order reactions were determined using the relation

$$\ln (a_1' - a_1) + k_1 t_1 = \text{constant},$$

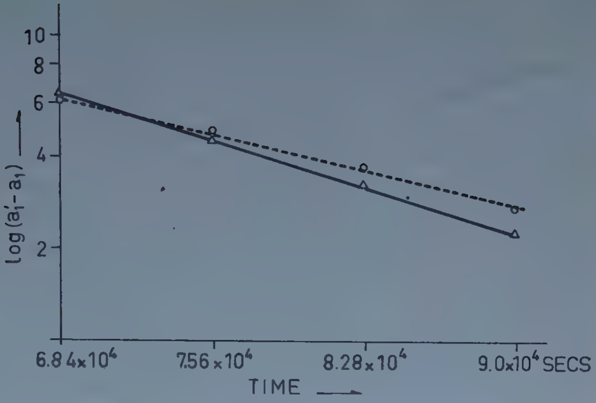


Fig. 9. A plot to determine the first order reaction rate constants of the two cases represented in Figs. 6, 7, and 8. Further explanations will be found in the text.

where a_1 = mole fraction of acetic acid at t_1, and a_1' = mole fraction of acetic acid at say $t_1 + \tau$ where τ is a big time interval; here τ was 6.48×10^4 sec. Several pairs of points were taken and plotted as in Fig. 9, from which the reaction rate constants k_{I} were determined from the slope of the straight line. The dotted straight line represents the case for the reaction in acetone medium at 22°C and the solid straight line that for the case of the pure reactants at 22°C.

The first order reaction rate constant for the hydrolysis of acetic anhydride at 22°C in presence of acetone (in a system of 12.75 g of acetic anhydride, 2.25 g of water and 2.25 g of acetone) was found to be 3.7×10^{-5} sec^{-1}. The first order reaction rate constant of the hydrolysis at 22°C is 4.5×10^{-5} sec^{-1}, and, taking its value at 27°C as 6.5×10^{-5} sec^{-1} from our earlier experimental observations, we can estimate the so-called activation energy of the reaction from the Arrhenius equation $\log k_1/k_2 = E/R\ (1/T_2 - 1/T_1)$, where k_1 and k_2 are rate constants at temperature T_1 and T_2 respectively. Our estimate of the activation energy of the reaction thus comes out to be 6.02 k cal per mole.

On the possible effect of a magnetic field on chemical reactions

In our previous communication, while comparing the experimental findings on the rate of the hydrolysis of acetic anhydride as followed by the help of the high resolution n.m.r. method, with those found by actual chemical experiment, we found that although there was fair agreement between the two experiments for a major part of the initial stage until the mole fraction of acetic acid formed was 0.5, some divergence towards the end of the reaction appeared, which seemed to show that the reaction as followed by the n.m.r. experiment has been enhanced as compared to the titration experiment. We have discussed some points regarding this divergence, especially the role of molecular association leading to the dimerisation of acetic acid and its bearing on chemical shift in n.m.r. experiments. Some other points we feel need consideration. In the n.m.r. experiment the sample containing the reactants and its subsequent products had all the time been in the magnetic field of a few thousand gauss of the permanent magnet used in our experiment. In the chemical experiment, however, no such field (neglecting, of course, the ever-present earth's magnetic field) was present. The question one may ask is this: Can there not be any effect of the magnetic field (of our permanent magnet) in the reaction observed by us by the n.m.r. method? It is well known that chemical reactions are essentially concerned with the electrons of atoms and molecules. If these electrons are endowed with spins and electrical and magnetic properties, it is not unnatural to think that the action of the magnetic field will have some effect on the freedom of these electrons in coming into chemical bonding.

The question whether magnetism would influence a chemical reaction or not had been earlier considered by investigators like Remsen, Nichols, Rowland and Louis Bell, Loeb, Wolff, Alexandre de Hemptinne, Bhatnagar and his collaborators and others.

According to A. de Hemptinne's argument [31], the magnetic field affects the equilibrium and velocity of reaction of any chemical system as follows. According to him, the heat of reaction of a chemical system is different in the magnetic field and outside the field. Now, the heat of reaction is related to the equilibrium constant by the equation $d \ln K/dT = q/RT^2$. If q is altered in the magnetic field, then K also is affected. Now the equilibrium constant is the ratio between the forward and backward velocity constants of the reaction. If K is affected by the magnetic field, the forward and the backward velocity constants are changed. However, Hemptinne stated that, although theoretically there is an effect of the magnetic field on chemical reaction, experimentally it is too small to be of much consequence. Bhatnager and his collaborators [32] have studied this question in some detail. According to them the magnetic field has the effect of altering the probability of inelastic collisions between two constituents which combine to make the final product. In a magnetic field, the atoms (and ions) assume discrete orientations, that is, they take up certain positions relative to each other. Thus it seems likely that collisions due to thermal agitation will take place in a more orderly and directed manner. This would result in changing the probability of inelastic collisions, which in its turn would affect the velocity of reaction.

Bhatnagar, Mathur and Kapur [32] showed also that in almost all earlier cases where negative results were obtained, the reasons may be ascribed to causes like the reactions studied proceeding with great velocity and that there was no appreciable difference between the susceptibilities of the initial reactants and the final products. They showed that in a homogeneous reaction, the velocity of reaction is accelerated, retarded, or unaffected by the magnetic field according as

$$\sum_f \chi_M \gtreqqless \sum_i \chi_M \qquad (1)$$

where $\sum_f \chi_M$ is the sum of the molecular suspectibilities of the final product and $\sum_i \chi_M$ is the sum of the molecular susceptibilities of the initial reactants.

Now, as the hydrolysis of acetic anhydride, studied by us by the n.m.r. method, is rather a slow reaction, if the magnetic field has some positive effect in altering the velocity of the reaction, the result of the effect would be more pronounced towards the end of the reaction. And whether it would be accelerated or retarded or not may be checked by the relation (1) above.

The specific susceptibilities of acetic anhydride, water, and acetic acid taken from the "International Critical Table" were multiplied by the respective molecular weights, and the resulting molar susceptibilities in cgs units are quoted below:

$$\chi_M\text{, acetic anhydride} = -52.734 \times 10^{-6},$$
$$\chi_M\text{, water} = -12.96 \times 10^{-6}$$
$$\chi_M\text{, acetic acid} = -31.56 \times 10^{-6}.$$

So in our case, since the final product is 2 moles of acetic acid,

$$\sum_f \chi_M = -63.12 \times 10^{-6} \quad \text{and} \quad \sum_i \chi_M = -65.12 \times 10^{-6}.$$

In the domain of diamagnetism, such a difference in χ_M (3 per cent) is considerable. Conclusions regarding molecular structure have been drawn from such differences as, for example, in the case of Keto-enol structure of ethyl benzol acetate where the diamagnetic susceptibilities of the two forms differ by 3.3 per cent. However, if the difference is less than 1 per cent it would be advisable not to draw any conclusion from it. Since in our case $\sum_f \chi_M > \sum_i \chi_M$, the reaction, according to the argument of Bhatnagar, Mathur and Kapur, would be accelerated. It is interesting to note that the divergence between the n.m.r. experiment with the reacting sample in the magnetic field and the chemical experiment (sample not in the magnetic field) seems to be in the right direction towards the end of the reaction. Our experiment, we believe, has shown an effect of the magnetic field on the velocity of a chemical reaction.

While discussing different questions of nuclear magnetic resonance vis-à-vis chemical conversion, it may not be out of place to point out the case where the magnetic moment of protons in water plays a catalytic influence on the spinisomerisation in the hydrogen molecule, the ortho-para conversion, in water.

Another question from the nuclear magnetic resonance point of view may come up for consideration. It is the energy exchange process of nuclear spin-lattice interaction in which radio-frequency absorbing nuclei give off the excess energy as thermal energy to the lattice comprising the molecular surroundings built up of the electron cloud. The related question is this, whether in such a heat exchange process the velocity of a chemical reaction can be altered or not. However, since the stimulating radio-frequency field was not present all the time, but was switched on from time to time only during the recording of signals, it is very probable that the thermal relaxation process of nuclear spins has not influenced the velocity of the chemical reaction.

Let us now refer our arguments concerning the effect of a magnetic field on the velocity of a chemical reaction to the case of the reaction between methyl alcohol and acetic anhydride leading to the final product of methyl acetate and acetic acid.

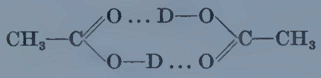
Here χ_M, methyl alcohol at 27°C $= -21.85 \times 10^{-6}$; χ_M, acetic anhydride $= -52.734 \times 10^{-6}$; χ_M, methyl acetate $= -43.66 \times 10^{-6}$; and χ_M, acetic acid $= -31.56 \times 10^{-6}$. Here $\sum_f \chi_M = -75.22 \times 10^{-6}$ and $\sum_i \chi_M = -74.58 \times 10^{-6}$ (all values expressed in cgs units as before).

Here the difference is only 0.64×10^{-6}, which amounts to 0.8 per cent only and it is safe not to draw any conclusion based on this small difference. It is very likely that the influence of the magnetic field would not be pronounced in this case. It may be pointed out that, in the case of the hydrolysis of acetic anhydride, the difference in question $(\sum_f \chi_M - \sum_i \chi_M)$ differs from that in the case of the reaction between methyl alcohol and acetic anhydride by nearly a factor of four.

We shall close the discussion of this section by saying a few words on diamagnetic susceptibility of some substances in relation to their molecular association. Although diamagnetism is generally independent of temperature, it has been found that diamagnetic susceptibility varies slightly with temperature only for those compounds which are said to be associated liquids (33) and investigators in this field ascribe the changes in diamagnetic susceptibility to changes in molecular association. One of the causes of the difference in diamagnetic susceptibilities between initial reactants and final products for the two cases mentioned above may be due to the fact that in the case of the first reaction the product is entirely an associated liquid (2 moles of acetic acid), whereas in the second case only one of the products (1 mole of acetic acid) is an associated liquid while the other one, methyl acetate, is not. Moreover in the second case one of the reactants is methyl alcohol which is more an associated liquid than water used in the first case. From the molecular association point of view it seems that, if in the process of a chemical reaction, there is an essential difference in character in regard to molecular association of the reactants and products, then $\sum_{f} \chi_M$ and $\sum_{i} \chi_M$ will differ appreciably, and on those reactions the magnetic field will have a positive effect, but otherwise not.

Some notes on heavy acetic acid

While discussing the various questions related to the n.m.r. experiment of following the the hydrolysis of acetic anhydride, another interesting question has occurred to us. We have said that the final product of acetic acid exists in the dimerised state. If now, instead of ordinary water (H_2O) we take heavy water (D_2O) for the hydrolysis of acetic anhydride, then double molecules of heavy acetic acid would be formed and, according to the molecular arrangement, the deuterons will exist in the deuterium bridge O–D...O as in



It is evident that there will be an electric field gradient at the position of the deuteron since the nature of the bonds by which the oxygen atoms are bonded to the deuteron are not the same, the deuterons may manifest pure nuclear electric quadrupole resonance. It may be worth while to look for deuteron quadrupole resonance in heavy acetic at a low temperature quenching the random rotational molecular motion. A positive effect would thus place the generally well accepted view of dimerisation of acetic acid on a still firmer footing.

Proton chemical shift in acetic acid–heavy water system

We were interested to observe whether the proton chemical shift of the COOH peak in acetic acid gives the same nature of the curve in a system of acetic acid and heavy water, D_2O, as is presented in a system of acetic acid and ordinary water [4, 5]. This experiment with heavy water was done in a magnetic field of approximately 4930 gauss. The earlier experiment with ordinary water was done in a magnetic field of approximately 3285 gauss. Consequently the separation between chemically shifted resonance lines of interest to us was greater by a factor of $\frac{3}{2}$, and,

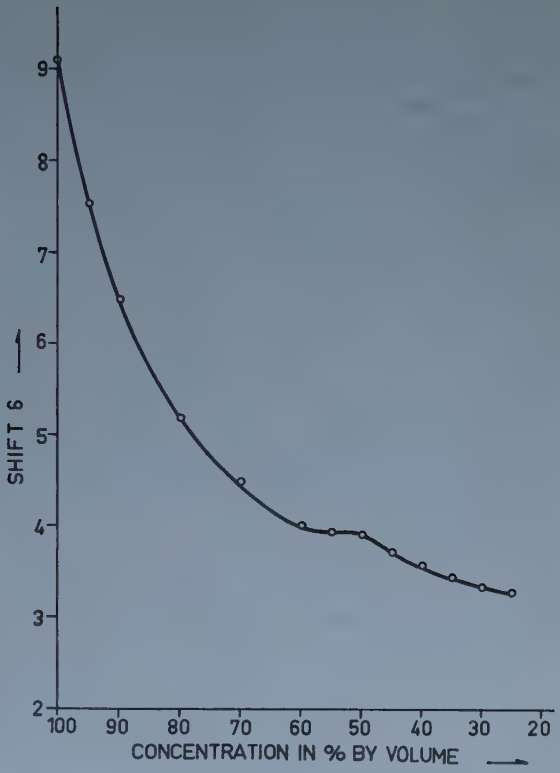


Fig. 10. The chemical shift of the COOH peak in the acetic acid–heavy water system measured from the CH_3 peak as reference and plotted against concentration in per cent by volume.

since the resolution was better in this case by at least a factor of five, the experimental errors are less than in the earlier experiment. When the proton chemical shift of the COOH peak from a system of acetic acid-heavy water was plotted against concentration of acid in per cent by volume, shown in Fig. 10, the same nature of the curve with a characteristic "hump" on it was obtained as in the case of the acetic acid–ordinary water system. We believe that the "hump" is due to alternative hydrogen bond formation between CH_3COOH and D_2O. This curve is made up of three contributions which affect the chemical shift of the proton in COOH group: (I) breaking up of the hydrogen bond of the double molecules of acetic acid, (II) alternative hydrogen bond formation with D_2O and (III) exchange of deuterons and protons.

It is resonable to believe that processes (I) and (II) will be predominant when the concentration of acetic acid is rather high while process (III) will be predominant when the concentration of acetic acid is rather low.

The ideas of hydrogen bond formation between acetic acid and water molecules which were presented in our earlier communication, seems to be in excellent agreement with the ideas which Fénéant [34] has expounded in the work entitled "Spectres Raman des solutions d'acide acétique dans l'eau". However, this work came to our attention after our n.m.r. studies were already published. This idea of molecular association between acetic acid and water is opposed to the idea of dissociation of acetic acid molecules, Fénénant proposes that, even in dilute solutions, one molecule of acetic acid and two molecules of water associate to form a 1:2 complex. The picture of molecular arrangement is, however, not presented here for the sake of brevity.

It will not be out of place to mention a few words about the analogy that we gave between the nature of this curve and p–v curves. Here, in the abscissa we have plotted the concentration of acid in per cent by volume, the solvent being water. We know that when a solute is dissolved in a solvent, the solute molecules behave as gas molecules. This picture is of course valid for dilute solutions as embodied in Vant Hoff's original work. However, this idea has led us to the analogy between "volume concentration" and "v" which appears in gas equations. Regarding the "chemical shift" (denoted here as δ) which is plotted along the ordinate and its analogous quantity pressure (p), it has occurred to us that pressure affects molecular association [14] in associated liquids. Now "chemical shift" is also dependent upon the extent of association. So "chemical shift" and pressure acting upon the liquid should not be unrelated. This consideration has led to correlate "chemical shift" (δ) and pressure (p). This analogy has prompted us to search for a relation between "chemical shift" (δ) and "concentration" (v) which may be covered by the relation $(\delta + r/v^2)(v - s) = \text{constant}$, where r and s are also constants, possibly here related to equilibrium constants of the acetic acid–water system, which may explain the cubic nature of the curve.

Referring to the proton signal of the COOH group in the acetic acid–heavy water system it constitutes a single line and is concentration dependent. The occurrence of a single resonance line and its concentration dependence shows that protons are present in two molecular species in rapid equilibrium. The life time of each molecular configuration exceeds the time of one nuclear Larmor precession at 5×10^{-8} sec for a field of 4930 gauss used here, but is short compared to the reciprocal of the frequency separation between otherwise two resonance lines appropriate for the diamagnetic shieldings for which the single line represents the weighted average. The experiment of proton resonance from a system of CH_3COOH and D_2O shows that the protons of COOH group are experiencing a diamagnetic shielding, the average of which would exist at the position of the protons in the COOH groups and at the position of the deuterons in D_2O. The same would be true for deuterons if one were looking for deuteron resonance. In other words, the protons of COOH group and deuterons of D_2O are experiencing the same diamagnetic shielding when a system of CH_3COOH and D_2O is placed in a magnetic field. It is therefore suggestive that, if in such a system the magnetic moment determination of deuteron with respect to proton is made by the resonance absorption method by simultaneously observing the proton signal of the COOH group and the deuteron signal from D_2O, then the diamagnetic shielding correction which would otherwise have arisen if two different molecules were taken, would not arise.

On H-bond shift and equilibrium constants in certain cases

The potentialities of the nuclear magnetic resonance method of studying chemical equilibria was first pointed out by Arnold, Dharmatti and Packard [3]. Recently Huggins, Pimmentel and Shoolery [24] have studied the hydrogen bonding of chloroform in solution and have determined the equilibrium constant of the chloroform–acetone and chloroform–trimethylamine systems from the chemical shift of the hydrogen bonded protons in chloroform. It has occurred to us that the procedure they have adopted to determine the equilibrium constant K for the one-to-one complex can be simplified by using only the experimental chemical shift *vs* concentration curve, instead of the laborious process of drawing other curves with different assumed values of K to fit the experimental curve. The procedure suggested is outlined below: The one-to-one complex between chloroform–trimethylamine is represented as

$$CCl_3H + N\,(C_2H_5)_3 = CCl_3H \cdot N\,(C_2H_5)_3$$

The equilibrium constant of the system K is given by

$$K = \frac{X\,(C+B-X)}{(C-X)\,(B-X)} \tag{1}$$

according to notations used by them. X = moles complex formed; C = moles chloroform originally present; B = moles base originally present. Out of the two values of X from eq. (1) only one is admissible taking into account that in the abscence of any base (solvent) no complex is formed (i.e. $X = 0$) and also in the limit of infinite dilution $C \to 0$ and $X \to 0$. Hence

$$X = \frac{(C+B) - \sqrt{(C+B)^2 - 4\,K\,C\,B/K+1}}{2}. \tag{2}$$

The value of X for $C = B$ is of special interest in that case

$$\frac{X}{C} = 1 - \sqrt{1 - K/K+1.} \tag{3}$$

Now, the general equation governing the observed chemical shift and quantities of free and complexed chloroform is given by

$$\nu' = X/C \cdot \nu_x + C - X/C \cdot \nu_c \tag{4}$$

where ν_c is the characteristic precessional frequency of protons in free chloroform; ν_x that in complexed chloroform, and ν' the observed resonance frequency. Eq. (4) is based on Gutowsky and Saika's theory of chemical shift discussed earlier.

In the limit of infinite dilution when $C \to 0$ and $X \to 0$ and $X/C - X = K$, if we denote ν' by $(\nu')_{c=0}$, then from eq. (4)

$$(\nu')_{c=0} = \frac{K\,\nu_x + \nu_c}{1+K}$$

or

$$\nu_x = \frac{(1+K)\,(\nu')_{c=0} - \nu_c}{K}. \tag{5}$$

Now, for the case $C = B$, let ν' be denoted by $\nu'_{\text{eq.}}$ and let us put the value of X/C as given by eq. (3) in eq. (4) whence

$$\frac{\nu_c - \nu'_{\text{eq.}}}{\nu_c - \nu_x} = 1 - \sqrt{1 - \frac{K}{K+1}}. \tag{6}$$

If we denote $1+K/(1+K)$ by α and put the value of ν_x from eq. (5) in eq. (6) we get

$$\frac{\nu_c - \nu'_{\text{eq.}}}{\nu_c - (\nu')_{c=0}} = \alpha\,(1 - \sqrt{1 - 1/\alpha}). \tag{7}$$

Now the quantity on the right hand side is the ratio between the difference of chemical shifts involving three points, and it is also apparent that this ratio is independent of whether the chemical shift is expressed in cycles/sec or in milligauss or by the parameter δ. If we denote this ratio by f we get $\alpha = f^2/(2f-1)$ or the equilibrium constant

$$K = (2f-1)/(f-1)^2 \tag{8}$$

Thus we can calculate K if we know the factor f without drawing different calculated curves with assumed values of K to fit the experimental curve.

From the experimental observations of Huggins, Pimmentel and Sholery on the chloroform–acetone and chloroform–trimethylamine systems we have evaluated f and have seen that the values of K thus calculated from eq. (8) agrees well with their stated K values for those systems. K, for chloroform–acetone system is 2.1 (calculated from our procedure above) compared to 1.8 from their determination. K, for the chloroform–trimethylamine system, is 3.1 (calculated from our procedure) compared to 3 from their determinations. This simplified procedure, however, is restricted in its application to one-to-one complexes and is not applicable to systems where dimerisation and higher polymerisation occur.

H-bond shift in formic acid

Hydrogen bonding and dimerisation in formic acid has been suggested earlier from studies of infrared and Raman spectra and electron diffraction studies. Mention should be made of Pauling and Brockway's [35] electron diffraction study from which they determined the dimeric structure of formic acid and the O–H...O distance of 2.67 Å. Electron diffraction studies have also thrown some light on the position of the hydrogen atom in O–H...O. The three atoms in a hydrogen bond lie in a straight line, the hydrogen atom being closer to one atom than the other. Evidence is given that when two oxygen atoms are hydrogen bonded the O–H...O distance is between 2.5 and 2.9 Å, and that the equilibrium position of the hydrogen atom is about 1.00 Å from one of the two oxygen atoms and 1.5 to 1.9 Å from the other. The high resolution n.m.r. studies possibly will not be able to give this information directly.

The proton signals from formic acid (HCOOH) consisted of two chemically shifted lines of nearly equal intensities. The chemical shift of COOH peak was measured from the methyl peak in acetone. The δ value of the COOH group of pure acid was 8.8. The δ values of protons in COOH group are therefore seen to decrease progressively from propionic acid (CH_3CH_2COOH, $\delta = 10.7$) acetic acid (CH_3COOH, $\delta = 9.1$) and formic acid ($HCOOH$, $\delta = 8.8$) as different groups ethyl and methyl groups are added to COOH.

The molecular complex formation between formic acid and acetone involving the hydrogen bond is revealed by the H-bond shift of COOH peak as depicted in Fig. 11.

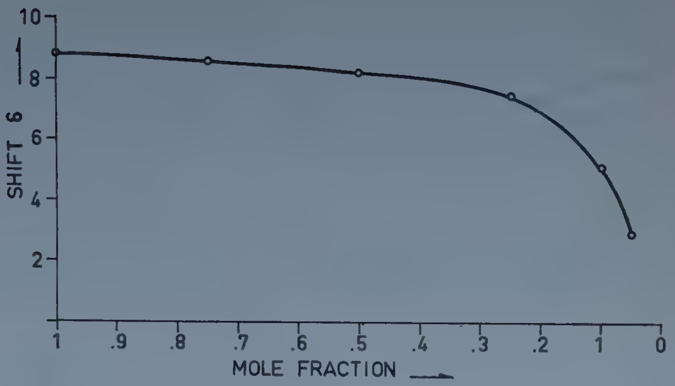


Fig. 11. The H-bond shift of proton resonance of formic acid in acetone solution.

It may be mentioned here that from H-bond shift of acetic acid–acetone system Huggins, Pimmentel and Shoolery [6] have made an interesting attempt to evaluate the difference in this shift due to a double molecule and a single molecule and to correlate it with the hydrogen bond energy. Although the attempt is encouraging, since the procedure involves assumption of values of different quantities, such as equilibrium constant of acetic–acetone system, it is necessary that these quantities be accurately determined.

Proton resonance in propionic acid

In a previous communication [5] we have suggested from the nature of the chemical shift curve of the COOH peak in the propionic acid–water system that propionic acid exists as double molecules by virtue of hydrogen bonding and can also enter into hydrogen bond formation with water. Any solvent affecting this bond by forming molecular complexes with it will also change the diamagnetic shielding of the protons in the hydrogen bond and will alter this H-bond shift. As in the case of the acetic acid–acetone system we have observed this shift in the propionic acid–acetone system. The proton resonance signals from pure propionic acid (CH_3CH_2COOH) is shown in Fig. 12, where the magnetic field increases from left to right. The proton peak due to the COOH group occurs at the lower value of the externally applied magnetic field, while the peaks due to CH_2 and CH_3 occur at higher values of the magnetic field. The splitting due to electron coupled spin–spin interaction of the protons in CH_2 and CH_3 is shown in the picture. If we denote CH_3, CH_2 and COOH groups by A, B, C, respectively, then the relative chemical shift expressed in terms of resonance frequencies ω_A, ω_B, ω_C, and the spin–spin interaction parameter (J_{AB}) are given by

$$\frac{\omega_A - \omega_B}{2\pi} = 26.2 \pm 1 \text{ cycles per sec.}$$

$$\frac{\omega_B - \omega_C}{2\pi} = 199 \pm 2 \text{ cycles per sec.}$$

$$\frac{J_{AB}}{2\pi} = 7.16 \pm 0.5 \text{ cycles per sec.}$$

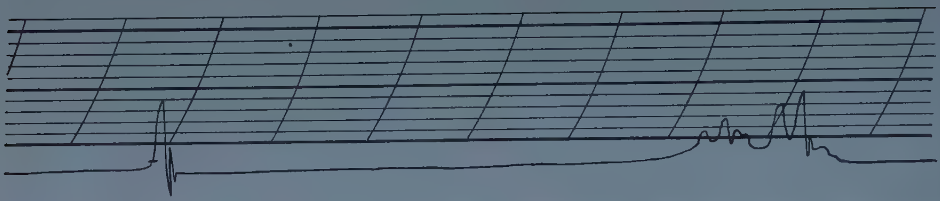


Fig. 12. Spectrum of propionic acid (CH_3CH_2COOH) sufficiently resolved to show the splitting due to indirect spin-spin coupling interaction between protons in CH_3 and CH_2 groups. The proton peak due to the COOH group, occurring at a lower value of the externally applied magnetic field, is shown at the left-hand side of the picture.

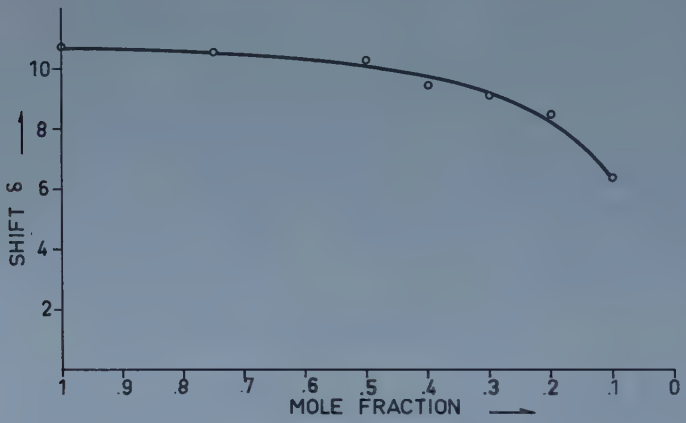


Fig. 13. The H-bond shift of proton resonance in propionic acid in acetone solution.

Here the spin–spin interaction parameter J of CH_3 and CH_2 seems to be equal to that in the case of CH_3 and CH_2 groups of ethyl alcohol as determined by Arnold [9], but the relative chemical shift (if expressed in terms of say δ), is less than that in the case of ethyl alcohol. This is due to the different electronegativities of the COOH and OH groups in propionic acid and ethyl alcohol respectively.

Here J is not $\ll \delta$ (compared to the case of ethyl alcohol, say), and as a result, asymmetry in the lines due to J-splitting and departure from Gutowsky's rule [36] may arise, which seems to be apparent in the picture.

The H-bond shift of the COOH peak in acetone solution is represented in Fig. 13. As in the case of acetic acid, we have observed that carbon tetrachloride has no influence on this shift. Carbon tetrachloride, however, profoundly affects the hydrogen bonding of ethyl, methyl and other alcohols. These n.m.r. observations thus also show that the nature of hydrogen bonding in carboxylic acids and alcohols is different, as we have mentioned earlier.

H-bond shift in methyl alcohol

The question of hydrogen bonding in methyl alcohol has been mentioned earlier in this communication, especially in connection with the studies of the kinetics of its reaction with acetic anhydride as followed by the n.m.r. method.

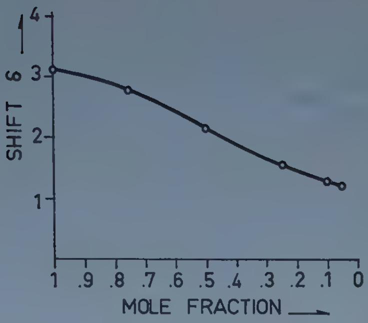


Fig. 14. The H-bond shift of proton resonance of methyl alcohol in acetone solution.

The chemical shift of the OH group of methyl alcohol was first observed by Arnold and Packard [29], and their experimental observations were interpreted by Liddel and Ramsey [37] from the point of view of hydrogen bonding of the methyl alcohol. Recently Cohen and Reid [38] have studied this shift in chloroform and carbon tetrachloride solutions. We have seen that acetone also affects the hydrogen bonding in methyl alcohol, and the H-bond shift, depending on dilution in acetone, is represented in Fig. 14. The shift was measured from the methyl peak of acetone.

On unimolecular transformation in acetylacetone

In a previous communication [39] we have described an experiment concerning keto and enol forms of acetylacetone (where the two molecular configurations differ in respect to the position of a hydrogen atom in the molecule), and have discussed some of the conditions regarding sweeping of the magnetic field and selection of peaks for area measurements in the high resolution n.m.r. trace of such a molecule. The signals with a better signal-to-noise ratio are given here in Fig. 15 for the purpose of our discussion below.

We shall now discuss here and describe an experiment on the keto–enol transformation in acetylacetone in the light of Gutowsky and Saika's theory of chemical shift, mentioned earlier. This transformation is strictly unimolecular since it is concerned only with a change from one molecular configuration to another. Now the rate of keto–enol transformation of acetylacetone seems to be fast. We have tried to observe this rate of transformation. Referring to the spectrum of acetylacetone in Fig. 15 and also to our previous communication, we know that at 26°C the enol content is 75% and that of keto is 25% at equilibrium (i.e. the equilibrium constant is 3). Now if we start with pure enol form (say 100% enol) the transformation to-

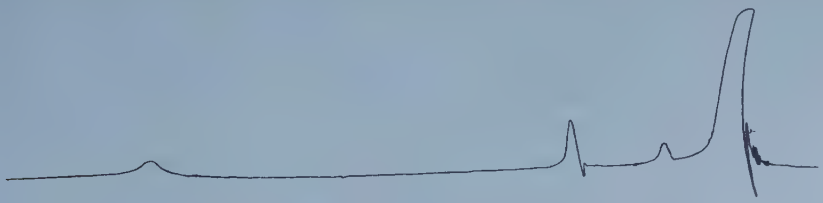


Fig. 15. Spectrum of acetylacetone resolved to show the internal chemical shift. The proton peak from the OH group of enol form of the molecule is shown on the left-hand side of the trace. The value of the externally applied magnetic field increases from left to right in the trace.

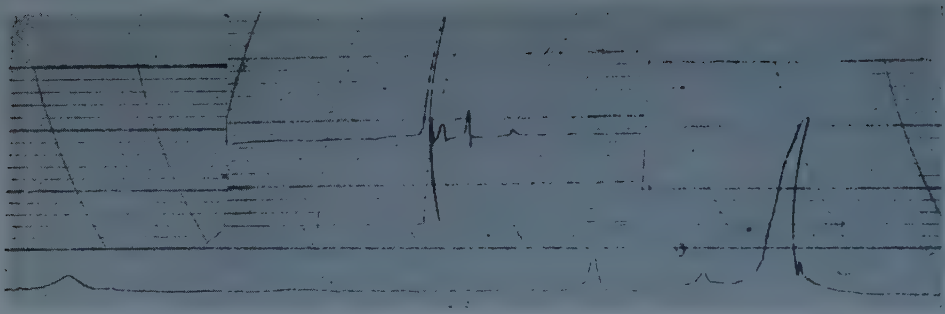


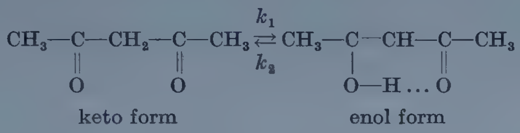
Fig. 16. Signal traces concerning the unimolecular transformation of acetylacetone. In the upper trace the magnetic field was swept rather rapidly through resonance from higher to lower values while in the lower trace it was slowly swept in the reverse direction. Further elucidation is set forth in the text.

wards equilibrium would change enol and also the keto by only 25%. On the other hand if we start with pure keto (say 100% keto) the transformation towards equilibrium value would change keto and also enol by 75%. So the latter procedure, viz. starting with pure keto and to reach the equilibrium, would be more likely to give a detectable picture of the keto–enol transformation. It may sound promising but there are some inherent difficulties in the experiment. This is because of the fact that the separation of the keto and enol forms had to be done first and the keto sample put in the sample tube of the n.m.r. probe. (The test tubes used were made of quartz and not of glass as the latter catalyses the transformation in question. When the liquid, contained in a quartz tube, is cooled in a mixture of acetone and dry ice the enol form mainly crystallises out at nearly −9°C and the remaining liquid is enriched in keto form).

This procedure of separation and putting the keto-enriched sample in the n.m.r. probe of the radio frequency bridge takes nearly two minutes and then for sweeping the magnetic field to get signals from OH (enolic), CH (enolic), CH_2 (keto) and CH_3 groups respectively (as it comes in sequence from left to right in Fig. 15) also takes appreciable time (the sweep time from OH peak to CH_2 peak takes nearly 30 seconds). Due to the time by which the sweep-field takes to pass from the OH peak to the CH_2 peak, one gets a signal of CH_2 keto peak which does not correspond to the equilibrium value at the instant when the OH peak was traced. If this is the state of affairs on slowly sweeping the field let us see what information we can get of this transformation if we quickly pass through the resonance lines just after putting the keto-enriched sample in the n.m.r. probe. Although this procedure gives some information on the transformation, one should not, as we have stated in our earlier communication, recommend this procedure for very accurate determination of keto–enol equilibrium. However, by putting the keto enriched sample in the n.m.r. probe and quickly sweeping the field from higher to lower values so that CH_2 keto peak comes earlier than enolic OH peak a third minute trace of the signals is obtained (as shown by the upper trace in Fig. 16) where the intensities of the CH_2 peak of keto form (second from the left in the upper trace) and of OH peak of enol form (extreme right in the upper trace) show that the keto content in the sample on the third minute is greater than the equilibrium value (at equilibrium the CH_2 peak should be less than OH). This proves that the keto–enol transformation is not complete in three minutes.

However, we have seen that this transformation is complete within five minutes. A fifth minute slow sweep trace (the lower trace in Fig. 16) shows that the areas under CH_2 and OH correspond to equilibrium values. The conclusion from repeated observations that the transformation is not complete within three minutes but is complete within five minutes may be examined in the light of Gutowsky and Saika's theory of chemical shift.

For the sake of discussion the structural formulae of keto and enol forms of acetylacetone are given below and we denote by k_1 and k_2 the rate of transformations from keto to enol and from enol to keto forms respectively. Evidently since the ratio of enol to keto contents at equilibrium is 3 (the equilibrium constant being 3) $k_1 = 3\,k_2$.



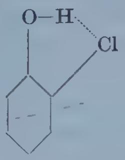
$$CH_3-\underset{\underset{O}{\|}}{C}-CH_2-\underset{\underset{O}{\|}}{C}-CH_3 \underset{k_2}{\overset{k_1}{\rightleftarrows}} CH_3-\underset{\underset{O-H\ldots}{|}}{C}-CH-\underset{\underset{O}{\|}}{C}-CH_3$$

keto form enol form

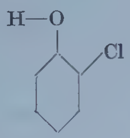
Now, as stated earlier, the two forms differ in respect of hydrogen atoms in CH and OH groups. When the enol form is transformed into keto form the hydrogen atoms of CH and OH groups constitute the CH_2 group. Now the appearance of two resolved chemically shifted resonance lines due to OH and CH group means that the transformation of the molecule from enol to keto form must be slower than the reciprocal of the frequency separation (say $1/f$). If the rate of transformation were faster than $1/f$ then there would not have appeared two different lines, according to Gutowsky and Saika's theory. Now since the rate of transformation from enol to keto is three times slower than the rate of transformation from keto to enol form, the latter must be slower than $3/f$ sec^{-1}. Here f is 194 cycles per sec and hence the rate of transformation from keto to enol form, which we were observing, must be slower than $3/194$ sec^{-1}. Now since it is a monomolecular transformation the half life must be greater than $(2.303 \log 2)/(3/194)$ sec or in other words the complete conversion from keto to enol must take more than 1.5 minutes. The observation that during the third minute the keto–enol conversion is not complete seems to be correct. Since we have observed that this conversion is complete within five minutes we can state that the rate of the keto–enol transformation of acetylacetone is approximately 5×10^{-3} sec^{-1}.

Some limitations of high resolution n.m.r. in studies of hydrogen-bonded systems

We should now discuss some limitations of n.m.r. method in studies of hydrogen bonding before we describe our observations on H-bond shift in acetylacetone. The observation of hydrogen bonding by infra-red and Raman spectroscopy and that by high resolution n.m.r. may have some characteristic differences as for example in the case of intramolecular hydrogen bonding of *o*-chlorophenol. Spectroscopic studies suggest that there are two molecular configurations, called *cis* and *trans* forms



cis form

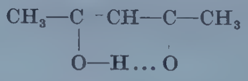


trans form

Now in the *cis* form there exists within the molecule hydrogen bonding between hydrogen and chlorine atoms (O–H...Cl) but such a bonding does not exist in the *trans* form. The infrared studies show two absorption peaks near about 7050 cm^{-1}. The area of one peak is about ten times than that of the other. The infrared spectrum shows that *o*-chlorophenol in carbon tetrachloride solution consists of about 91% *cis* and 9% *trans* molecules. We have observed that proton resonance in *o*-chlorophenol constitute a single line, although it is apparent that the diamagnetic shielding of protons in OH-group in the *cis* and *trans* forms should be different due to existence and non-existence of hydrogen bonding. N.m.r. studies, although they reveal the intramolecular hydrogen bonding [6] as it exists in the *cis* form, will not be able to reveal the existence of the two molecular configurations. This is because of the fact that the *trans* and *cis* forms of the molecules are in rapid equilibrium unlike the less rapid equilibrium of keto and enol form of acetylacetone discussed above. In brief, it may be stated here that the difference between the infrared and Raman spectroscopy and n.m.r. method in regard to study of hydrogen bonding is related to the life-times of molecular states. The vibrational period which is the limiting life-time of a molecule in the infra-red and Raman spectroscopy is of the order of 10^{-12} to 10^{-14} sec. while the limiting life-time of a molecule in the nuclear magnetic resonance is related to the nuclear Larmor precessional frequency and is of the order of 10^{-6} sec.

H-bond shift in acetylacetone

While locating the position of different chemically shifted lines it appeared to us that the chemical shift parameter ($\delta = 12.8$) of protons in the OH group (measured from the methyl peak) are not only greater here than the corresponding δ-values of the OH group in alcohols but also greater than the δ-values of the COOH group in acetic and propionic acids. In terms of diamagnetic shielding, the protons of the enolic OH group are much less shielded than protons in the OH group of alcohols or in the COOH groups of carboxylic acid. It occurred to us that this can only be possible if the oxygen atoms in enol form of acetylacetone enter into hydrogen bonding inside the molecule with the hydrogen atom containing the proton in question as depicted below:



$$\begin{array}{l} CH_3\text{—}C\text{ - }CH\text{—}C\text{—}CH_3 \\ \qquad\quad | \\ \qquad\quad O\text{—}H\ldots O \end{array}$$

Thus the enol form of acetylacetone gives an example of intra-molecular hydrogen bonding, which we mentioned earlier. Studies of intramolecular H-bonding by n.m.r. method have been reported only in the case of ortho chlorophenol by Huggins, Pimmentel and Shoolery [6].

We have observed that as in acetic and propionic acid acetone affects the hydrogen bonding in acetylacetone. The H-bond shift of the enolic OH group in acetone solution is represented in Fig. 17. It was, however, observed that as in the case of acetic acid the H-bonding in acetylacetone is not affected by carbon tetrachloride at acetylacetone concentration down to 20% by volume. At great dilution, although the methyl peak could be seen, the peak due to the OH group was nearly lost in the noise if the receiver gain was increased. In the case of acetone solution, however, it was noticed that unlike the shift in acetic and propionic acid the shift is accompanied

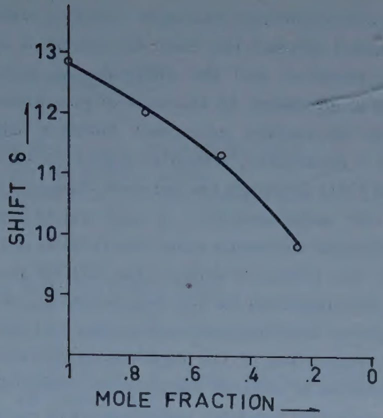


Fig. 17. The H-bond shift of proton resonance from the enol form of acetylacetone molecule in acetone solution.

by broadening of the OH peak. This shows that the equilibria between the complex of acetylacetone–acetone and molecules of free enol and keto forms are not so rapid, and according to Gutowsky and Saika's theory the line will be broadened.

We shall make a few more remarks related to the chemical shift of protons in the enolic OH group. Now since in heavy water the protons of the enolic OH group and deuterons exchange, similar arguments given here earlier in the case of acetic acid–heavy water system will show that the protons and deuterons concerned will experience the same diamagnetic shielding when such a system is placed in a magnetic field. Thus a simultaneous observation of proton resonance of enolic OH peak and deuteron resonance will serve to evaluate the deuteron–proton magnetic moment ratio with elimination of the diamagnetic shielding and other corrections [40, 41].

SUMMARY

The role of the high resolution nuclear magnetic resonance technique in the studies of proton resonance in so-called hydrogen bonded systems, where a hydrogen atom plays an all-important part leading to the phenomenon of "molecular association", is discussed in the context of earlier studies of this phenomenon by other physical methods such as infra-red, Raman spectroscopy, dielectric and electric dipole moment measurements of molecules, etc. Several nuclear magnetic resonance (n.m.r.) experiments are described concerned with the "chemical shift" (termed the H-bond shift) of the resonance line of the protons in such hydrogen bond. Gutowsky and Saika's theory of "chemical shift" is discussed with its bearing on some experimental observations. The application of the high resolution n.m.r. method to follow the kinetics of chemical reactions, which was demonstrated earlier, has been extended to follow the reaction between methyl alcohol and acetic anhydride. This reaction, as shown by the analysis of the n.m.r. data, is found to be a second order one with a reaction rate of 1.2×10^{-5} sec^{-1} molality^{-1} at 27°C. The effect of temperature and retarding effect of molecular complex forming solvent on the rate of the hydrolysis of acetic anhydride has been investigated at 22°C and in presence of acetone. The H-bond shift in acetic acid–acetone system has also been observed.

The possible effect of a magnetic field on chemical reactions as followed by the nuclear magnetic resonance method is also considered here in discussing the experimental findings of n.m.r. and chemical methods.

The intermolecular hydrogen bonding which exists in the case of formic acid, propionic acid and methyl alcohol has been investigated by this method by observing the H-bond shift in acetone solution, and the difference in nature of hydrogen bonding in carboxylic acids and alcohols is discussed. In the case of propionic acid (CH_3CH_2COOH), the electron-coupled proton spin-spin interaction parameter between CH_3 and CH_2 groups ($J/2\pi$) has been found to be 7.16 ± 0.5 cycles/sec., which is found to be equal to the corresponding $J/2\pi$ in ethyl alcohol (CH_3CH_2OH) although the relative chemical shift parameters (δ) of the two groups are different in the two molecules.

A deuteron exchange experiment with the acetic acid–heavy water system has been made to observe the chemical shift of the COOH proton peak and from the n.m.r. observations possibilities are suggested for the determination of the deuteron–proton magnetic moment ratio where diamagnetic shielding correction does not come into account.

The application of the high resolution n.m.r. method to the determination of the molecular configuration of organic compounds which differ in respect to the position of a hydrogen atom in the molecule has been investigated in case of acetylacetone, and the intramolecular hydrogen bonding which exists in the molecule has been investigated by observing the H-bond shift of the enolic OH protons. An experiment to follow the transformation from one molecular configuration to the other is described and the observations are discussed in the light of Gutowsky and Saika's theory. The unusually low diamagnetic shielding of protons in the enolic OH-group is observed and a deuteron–proton exchange experiment is also suggested in this system for deuteron–proton magnetic moment ratio determination eliminating the diamagnetic shielding correction.

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